

Pneumatosis Coli Associated to Severe Intestinal Graft Versus Host Disease Following Hematopoietic Cell Transplantation: Risk Factors and Dismal Outcome

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Pneumatosis coli (PC) is defined as the presence of air in the intestinal wall and is a significant complication of gastrointestinal (GI) graft-versus-host disease (GVHD) following hematopoietic cell transplantation (HCT). To better define risk factors for the development of PC and its outcome, we conducted a retrospective study in patients who developed severe GI GVHD after allogeneic transplant.

From January 2005 to December 2010, 470 related and unrelated HCT were realized at Maisonneuve-Rosemont Hospital. Of this group, 103 patients (21.9%) developed grade III to IV aGVHD. This study examines 91 of these 103 patients (88%). 12 patients with grade III to IV aGVHD (11.6%) were diagnosed with PC by tomodensitometry. This study compares the clinical characteristics, treatment and evolution of these 12 patients with PC with the control group of 91 patients with severe GI GVHD without PC.

All patients (100%) who developed PC received oral ciprofloxacin at the time of HCT compared with 42 patients (53.2%) in the control group. Donor and recipient CMV status were negative in 75% of patients with PC compared to 35.4% in patients with severe GVHD without PC. The median time of onset for acute GVHD was 64 days in the PC cohort (84 days control group). The median time for PC development was 199 days from HCT. Stem cell donors were female in 72.7% of patients with PC (47.3% in the control cohort). Sex mismatch between donor and recipient was present in 50%, (26% in the control group). 92% of patients received peripheral blood as their source of stem cells (82.2% in the no PC cohort). HLA disparity was present in 33.2% of patients with PC (15.2% in the no PC cohort). 41.7% of patients developed GI tract infections before the onset of PC (29.1% control group).

All patients were on calcineurin inhibitors at time of acute GVHD onset. Treatment of aGVHD consisted of corticosteroids MP 2 mg/kg in 91.7% of PC cohort (65.8% in the control group). The successive lines of treatment were: MMF 66.7% (78.5% in the rest of the cohort), daclizumab 75% (34.2% in the control group) and pentostatin 41.74% (5% in the no PC cohort) with complete resolution of GVHD symptoms in 16.7% (32.9% in the rest of the cohort).

PC is a severe complication of early onset GI GVHD. Risk factors included HLA disparity between donor and recipient, female donor, high dose and prolonged corticosteroids treatment for GVHD. GI tract infection may contribute to its

pathophysiology and frequently preceded PC onset. Anti-bioprophylaxis with ciprofloxacin was a statistically significant risk factor for PC development. Oral cipro for GI tract decontamination is suboptimal and should be revised. Treatment of GI GVHD with daclizumab or pentostatin increase PC risk. CMV seronegativity was not protective. GVHD related PC is associated to a high mortality rate (75% in the PC cohort and 59% no PC group) not statistically different from the dismal outcome of steroid refractory aGVHD.

Chronic GVHD-Associated Serositis and Pericarditis

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Background: Serositis and pericarditis are rare manifestations of chronic GVHD. No risk factors or predictive biomarkers associated with this syndrome have been recognized to date, and outcomes have not been described in large series.

Methods: In an effort to better characterize this condition, we searched our institutional database of allogeneic HCT occurring at OHSU between 1996-2012 for pts identified as having serositis with or without pericarditis. We reviewed clinicopathologic data to identify a cohort of patients who clearly had this complication in association with chronic GVHD. Laboratory studies from 1 month prior to diagnosis, at diagnosis, and 1 month post-diagnosis of serositis +/-pericarditis, as well as outcomes from invasive procedures, were included in our review.

Results: 894 allogeneic HCT procedures took place during the study time frame. 23 cases were identified in the database search, although 8 were not included in the final analysis (1 acute GVHD, 2 anasarca without clear serositis, 1 pre-transplant pericarditis, 1 malignant effusion, 3 HCT or majority of care elsewhere). 15 met criteria for having cGVHD-associated serositis or pericarditis: 14 were male pts, and 10 received Cy/TBI conditioning. All but 1 pt had a prior diagnosis of chronic GVHD. The complication occurred in the setting of recent immunosuppression (IST) taper in 12 of the cases. A significant increase in blood monocytes (median 500 vs. 1000 cells/uLP = .002) and decrease in serum albumin (median 3.4 vs. 2.65, P = .005) were identified at diagnosis compared with those values at one month pre-diagnosis. 13 of 15 pts were treated with steroids, with 7 of those demonstrating partial or complete response. 6 patients required invasive interventions (1 pericardiocentesis, 3 pericardial windows, and 2 pericardial stripping) due to severe symptoms. 3 pts died due to chronic GVHD complications.

Conclusions: These data suggest that chronic GVHD-associated serositis with or without pericarditis occurs mainly in the setting of treated as opposed to *de novo* chronic GVHD, frequently in the setting of IST taper. A notable predominance of male recipients receiving myeloablative TBI-based conditioning were identified in this cohort. Biomarkers that appear to be associated with the syndrome include a decrease in albumin and an increase in absolute monocyte count. Outcomes data from larger series are required to better understand the role of invasive procedures and optimal treatment for this rare complication.